REMARKS

Claims 1 – 5, 7 – 9, 13 – 18, and 20 are currently pending. Claims 1 and 20 are the pending independent claims. In the Office Action, Claims 1 – 5, 7 – 9, and 12 – 18 were rejected under Section 112, first paragraph as allegedly failing to comply with the written description requirement. Claim 18 was also rejected under Section 112, first paragraph, as allegedly failing to comply with the enablement requirement. Claims 1 – 5, 7 – 9, and 12 – 18 were also rejected under Section 112, second paragraph as allegedly being indefinite. Finally, Claims 1 – 5, 7 – 9, and 12 – 18 were rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,705,190 to Broad et al. ("Broad"), in view of the Ansel et al. publication in Pharmaceutical Dosage Forms and Drug Delivery Systems ("Ansel") and U.S. Patent 6,890,890 to Kirschner et al. ("Kirschner").

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. The Written Description Rejection.

The Examiner argues that Claims 1 – 5, 7 – 9, and 12 – 18, as amended previously, contain impermissible new matter, and therefore do not satisfy the written description requirement. The Examiner specifically objects to the limitation "wherein at least about 90% of the micronized clarithromycin particles are about 30μm or less in size" in Claim 1 as not being disclosed in the specification.

It is true that the words "at least about 90% of the micronized clarithromycin particles are about 30μm or less in size" are not recited ipsis verbis in the specification; however, the specification does clearly describe "micronized clarithromycin with a particle size from d(0.9) up to about 30μm" at page 5, last paragraph. Any person of ordinary skill in the pharmaceutical arts would readily equate this statement with the claim limitation "at least about 90% of the micronized clarithromycin particles are about 30μm or less in size", and know exactly where this claim limitation is supported in the

specification. When characterizing particle size distributions, notations such as "d(0.5)" and "d(0.9)" are commonly used to indicate particle diameters which comprise 50% or 90% , respectively, of the overall particle size distribution. This is a conventional shorthand way of designating a certain percentage of a substance having a certain diameter, well-known to scientists, engineers, and chemists who work on particulate formations fro pharmaceutical compositions. See, for example, U.S. Patent No. 6,696,086 (copy attached) at column 2, lines 65 – 66 which states that "D(0.9) denotes a particle size wherein 90% (volume) particles in the substance used are below D(0.9)." Thus, it is apparent that a person of ordinary skill in the art would readily discern that the limitation "at least about 90% of the micronized clarithromycin particles are about 30μm or less in size" corresponds to what is described and enabled at page 5, last paragraph.

Nonetheless, in order to avoid arguing over minor matters such as this, Applicants have amended Claim 1 to recite instead that the micronized clarithromycin particles have a particle size d(0.9) of about 30μm. In view of this, it is submitted that the written description rejection of Claim 1, and its dependent claims, should be withdrawn.

The Examiner also argues that the limitation of "a capsule" in Claims 17 and 18 does not comply with the written description requirement. It is respectfully submitted that these rejections are not well taken. The Applicants' specification clearly indicates that the micronized clarithromycin particles may be incorporated into either a tablet or a capsule. For instance, at page 6, second paragraph, it is stated that the dried clarithromycin may be used in the preparation of a dry mixture for either "tabletting or encapsulating." Likewise, at page 6, third paragraph, it is stated that the composition is "blended and tabletted or encapsulated." It is undisputable that a person of ordinary skill in the pharmaceutical arts would readily recognize these statements as describing both tablets and capsules incorporating the micronized clarithromycin particles as an active ingredient. Accordingly, it is submitted that the written description rejections of Claims 17 and 18 are improper and should be withdrawn.

II. The Enablement Rejection.

The Examiner contends that Claim 18 lacks enablement under Section 112, first paragraph. The Examiner alleges that the claim refers to "*preventing all diseases*" (emphasis from Office Action). However, the Examiner acknowledges that the claim is enabled for "treating diseases treatable with clarithromycin." Accordingly, the Applicants have amended Claim 18 to recite that the formulation is used in medicine for the treatment of diseases and the limitation regarding "prevention" of diseases has been deleted. In view of this amendment, it is respectfully submitted that the enablement rejection has been overcome and that the same should now be withdrawn.

III. The Indefiniteness Rejections.

The Examiner argues the limitation "at least about 90%" renders Claim 1, and its dependent claims, indefinite. Without acknowledging the propriety of this rejection, Applicants note that the qualifier "at least" has been deleted from Claim 1 as a part of the amendment discussed above in Section I. Claim 1 now recites that the micronized clarithromycin particles have a particle size d(0.9) of about 30μm. In view of this amendment, the indefiniteness rejection is moot, and should now be withdrawn.

IV. The Prior Art Rejections.

Finally, the Examiner contends that Claims 1 – 5, 7 – 9, and 12 – 18 would have been obvious to a person of ordinary skill over Broad in view of Ansel and Kirschner.

Looking first at Claim 1 and its dependent claims, as the Applicants have stressed before, Claim1 requires, among other things, an active substance comprises micronized clarithromycin, having a particle size d(0.9) of about 30μm. In other words, Claim 1 recites that 90% of the micronized clarithromycin particles have a particle size of about 30μm or less.

Broad, said to be the primary reference, discloses nothing about the use of "micronized" particles, a point the Examiner appears to acknowledge. However, he

attempts to fill in this missing disclosure by resort to Ansel and Kirschner. This is unavailing. Ansel is a general purpose textbook-type reference, which mentions that some pharmaceutically active ingredients have been "micronized," but provides no suggestion or teaching to micronized clarithromycin. Applicants do not claim to have invented the idea of "micronization." The mere fact that micronization technology was known to sometimes be used for pharmaceutical ingredients is hardly a suggestion to provide micronized clarithromycin particles in an otherwise novel combination of materials in a medicament formulation as specified in the present claims obvious.

As for the Kirschner reference, it is to be noted that, as amended herein, Claim 1 is directed to micronized clarithromycin particles which are intended for use in cores for tablets or capsule, i.e., dosage forms which will be taken orally. In contrast, Kirschner reference discloses an emulsion for a vaginal drug delivery system. *See, e.g.*, Kirschner, column 3, lines 50 – 53 and Claim 1. Clearly the dissolution issues and other factors pertaining to delivery and efficacy of an oral composition and one made for vaginal delivery are like "night and day." Hence, Kirschner's vaginal drug delivery system would not have provided any guidance to one of ordinary skill in the art regarding particle sizing for an oral dosage form of the pharmaceutical.

In addition to the foregoing, Claim 1 is also amended herein to specify that the micronized clarithromycin particles are dried to a final humidity of about 2.5%. None of the three cited references (neither Broad, nor Ansel, nor Kirschner) discloses drying micronized clarithromycin particles to a final humidity of about 2.5%.

Accordingly, Applicants respectfully submit that Claim 1 and its dependent Claims 2 – 5, 7 – 9, and 13 – 18, patentably distinguish over the cited references of Broad, Ansel, and Kirschner in that neither the "combination" of these references in the manner imaged nor any teaching of the references in combination would have been obvious to a person of ordinary skill in the art.

With regard to Claim 20, this claim also specifies a tablet core comprising micronized clarithromycin. As discussed above with respect to Claim 1, the Broad

reference does not teach micronized clarithromycin and neither Ansel nor Kirschner would have led one of ordinary skill in the art to substitute micronized clarithromycin in Broad's composition.

Further, Claim 20 species that the table core is a coated with a film coating which is applied as a fluid comprising a first film-forming agent having a viscosity of up to about 6 mPas together with at least 10% of a second film-forming agent having a viscosity of over 6 mPas and up to about 15 mPas. Applicants have found that the use of such film-forming agents in combination provides a more rigid and effective film coating for tablet cores in accordance with the present invention. The Examiner attempts to address these limitations by noting that both hydroxypropyl cellulose and hydoxypropyl methycellulose are mentioned in Ansel. The Examiner asserts that these are the same film-forming agents claimed in the current application and would thus inherently possess the same viscosity ranges. This assertion is incorrect in at least two aspects.

First, in the present application, Applicants do not merely disclose HPMC. They disclose a first HPMC having a viscosity of 6 mPas and a second HPMC having a viscosity of 15 mPas. *See* Example 5.

Second, the term "hydroxypropyl cellulose" does not refer to merely a single chemical compound; it refers to an entire class of polymeric compounds having a wide range of molecular weights, inherent viscosities, and other varying properties. Likewise, the term " hydoxypropyl methycellulose" also refers to an entire class of compounds having a range of varying physical properties. This point is well-evidenced. As noted before, the Lui reference previously cited by the Examiner (U.S. Patent No. 5,009,895) discloses various hydroxypropyl methycellulose (HPMC) compounds having viscosities ranging from 4 cps to 100,000 cps, depending upon the composition of the HPMC. Thus, a mere reference to " hydoxypropyl cellulose" or to " hydoxypropyl methycellulose", without any further qualification (as in Ansel), is insufficient to teach or suggest a particular structure of the polymer, the molecular weight of the polymer, or the viscosity of the polymer that would be effective for a particular application.

Accordingly, Claim 20 patentably distinguishes over the cited references of Broad, Ansel, and Kirschner for this reason as well.

In light of the foregoing, the present amendment is believed to place the application in a condition for allowance and entry of the foregoing amendments and allowance of Claims 1 – 5, 7 – 9, 13 – 18, and 20 is respectfully solicited.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our **Deposit Account No. 12-2355.**

Respectfully submitted,
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